Journal of the American College of Cardiology
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Published by Elsevier Science Inc.

Vol. 37, No. 1, 2001
ISSN 0735-1097/01/$20.00
PII S0735-1097(00)01060-3

Improvement of Afterload Mismatch of Left Atrial Booster Pump Function With Positive Inotropic Agent

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OBJECTIVES The objective of this study was to examine the hypothesis that a positive inotropic agent improves left ventricular (LV) filling during left atrial (LA) contraction in the presence of markedly elevated LV filling pressure.

BACKGROUND In patients with old myocardial infarction (MI), an increase in the operational LV chamber stiffness reduces LV filling during the LA contraction, resulting from an "afterload mismatch" of the LA booster pump function.

METHODS We investigated the effect of dobutamine infusion (3 μg/kg/min) on the LA pump function in the presence of elevated LV filling pressure induced by aortic constriction (Aoc) during acute MI in 10 dogs. Transmitral flow velocity was determined by transesophageal echocardiography, LV pressure by a micromanometer and LV volume by a conductance catheter. We measured the early (E) and late (A) diastolic peak transmitral flow velocities (cm/s) and LV chamber stiffness ($\Delta P/\Delta V$: mm Hg/ml; where ΔP is developed pressure and ΔV is the absolute filling volume during LA contraction).

RESULTS When the $\Delta P/\Delta V$ was increased by Aoc during MI (from 1.1 ± 0.8 to 3.1 ± 2.6 mm Hg/ml, $p < 0.01$), A decreased significantly (from 30 ± 5 to 22 ± 8 cm/s, $p < 0.01$), and the ratio of E to A increased (from 1.0 ± 0.3 to 1.4 ± 0.8, $p < 0.05$) compared with MI without Aoc, showing the pseudonormal transmitral flow pattern, the so called "LA afterload mismatch." Dobutamine under this condition significantly reduced the $\Delta P/\Delta V$ (to 1.7 ± 1.2 mm Hg/ml, $p < 0.05$), resulting in an increase in A (to 31 ± 8 cm/s, $p < 0.01$) and a decrease in E/A (to 1.0 ± 0.3, $p < 0.05$), and the transmitral flow became a prolonged relaxation pattern as in MI without Aoc in all dogs. There was an inverse correlation between the $\Delta P/\Delta V$ and the time-velocity integral of A ($r = -0.70$, $p < 0.01$).

CONCLUSIONS Dobutamine improved the afterload mismatch of the LA booster pump function. This effect may have been due to the reduction in LV operational chamber stiffness, resulting in an increase in the LA forward ejection into the LV. (J Am Coll Cardiol 2001;37:270–7) © 2001 by the American College of Cardiology

Atrial booster pump function plays an important role in the left ventricular (LV) filling, particularly in patients with early LV diastolic dysfunction in whom an increase in left atrial (LA) contraction results in the maintenance of LV filling and a normal cardiac output (1,2). The mitral flow velocity pattern, as determined by pulsed Doppler echocardiography in such patients with early diastolic dysfunction, reveals a decreased early diastolic velocity (E wave) and an increased late diastolic velocity (A wave). However, when the severity of LV diastolic dysfunction increases, a different pattern of LV diastolic filling is observed, which is called "pseudonormal," indicating a reversal of the abnormal ratio of mitral E and A wave velocities (2,3). When this occurs the increased LA contribution to LV filling as a compensatory mechanism in response to reduced early filling is lost, and a decrease in the mitral A wave is observed. An optimal therapy for these patients would be a medication that would increase the reduced efficiency of LA booster pump function in the presence of diastolic dysfunction.

The data on LA pump function, particularly in relation to elevated LV end-diastolic pressure have been reported from the labs of Hoit, Kawamura and Toutouzas (4–6). We have previously demonstrated that, in patients with old myocardial infarction (MI), the increase in the operational LV chamber stiffness at end-diastole induced by an acute pressure load significantly reduced LV filling during LA contraction, resulting from an "afterload mismatch" of the LA booster pump function (7).

It was hypothesized that a reduction in LV chamber stiffness produced by a positive inotropic agent improves LV filling during LA contraction in the presence of markedly elevated LV filling pressure. The aim of this study was to examine the effects of dobutamine (DOB) on LA booster pump function in dogs with pseudonormalization of the transmitral flow velocity pattern due to an afterload mismatch between the LA and the LV during atrial contraction.

METHODS

Animal preparation and data collection. Ten adult mongrel dogs weighing between 9 and 17 kg (mean 12.4 kg)

From the Second Department of Internal Medicine, Yamaguchi University School of Medicine, Yamaguchi, Japan. Supported, in part, by research grants 07670785 from the Ministry of Education, Science and Culture of Japan. Presented, in part, at the 43rd Annual Scientific Sessions of the American College of Cardiology, Atlanta, Georgia, 1994.

Manuscript received February 28, 2000; revised manuscript received July 24, 2000, accepted September 11, 2000.

Abbreviations and Acronyms

A = late diastolic transmitral flow velocity
Aoc = aortic constriction
DOB = dobutamine
E = early diastolic transmitral flow velocity
LA = left atrium/left atrial
LV = left ventricle/left ventricular
MI = myocardial ischemia/myocardial infarction
PV = pulmonary vein/pulmonary venous
(+) = with
(−) = without

were sedated with morphine sulfate (3 mg/kg subcutaneous) 30 min before the induction of general anesthesia with α-chloralose (30 mg/kg intravenous). They were ventilated with a Harvard respirator; the concentration of inspired oxygen and the ventilation rate were adjusted to maintain blood gases within the physiologic range. The chest was opened laterally through the fifth left intercostal space, and the pericardium was incised parallel to the phrenic nerve and opened. The heart was placed in a pericardial cradle. The sinus node was crushed, and a pacing wire was sutured on the LA appendage to keep the heart rate constant at 100 beats/min.

One micromanometer-tipped catheter (model PC-484A, Millar Instruments, Houston, Texas) was placed in LA through an incision in the LA appendage, and another was placed in the LV across the aortic valve via the left carotid artery. To ensure the accuracy of pressure measurements, the micromanometers and a fluid-filled transducer (Statham P23ID, Statham Instruments, Oxnard, California) were balanced, calibrated with a mercury manometer and adjusted for equal gain before insertion. The fluid-filled transducer, which was positioned at the midthoracic level, was balanced to atmospheric pressure to serve as the pressure baseline. The zero shift during the procedure was adjusted by comparing pressures, measured simultaneously by the fluid-filled lumens connected to the fluid-filled transducer. We confirmed that LV and LA diastolic pressures were identical during late diastasis. At the end of the experiment, the catheters were withdrawn and exposed to air to confirm the accurate registration of zero pressure.

To obtain the LV volume, an 8-pole electrode conductance catheter (Leycom, Netherlands) was introduced into the LV from the apex guided by two-dimensional transesophageal echocardiography and positioned along the long axis with the distal tip beneath the subaortic valve. The catheter was connected to a stimulator/signal processor (Sigma 5, Leycom, Netherlands). For catheter placement we examined each segmental pressure-volume loop to confirm that all segments were intracavitary and displayed a normal counterclockwise pressure-volume resurgence. The conductance catheter technique, which is based on the fact that changes in blood conductance in the LV are proportional to changes in LV volume, has been previously described (8). A fluid-filled catheter was placed in the pulmonary artery to calibrate the volume signal. Calibration was performed by the hypertonic saline technique (8), and saline was rapidly injected into the pulmonary artery at the end of expiration.

A pair of ultrasonic crystals (3-MHz, 2.5 mm in diameter) were attached face-to-face on the surface of the LA anterior and posterior walls to measure LA diameter.

The transmitral flow velocity was measured by transesophageal pulsed Doppler echocardiography using an ultrasound system (Aloka, Japan) with a 5-MHz Doppler transducer. The sample volume was placed between the mitral leaflets in the transesophageal four-chamber view.

Finally, one occluder was positioned around the descending aorta a few centimeters above the level of the diaphragm for the increase of afterload, and another occluder was placed around the proximal portion of the left anterior descending coronary artery to produce acute regional MI.

Experimental protocol. Pseudonormalization of the transmitral flow velocity pattern was produced by aortic constriction (Aoc) using the occluder during acute MI. The protocol consisted of three stages. First, data were acquired at baseline. Second, acute regional MI was produced by occluding the left anterior descending coronary artery. Recordings were made before and after Aoc about 15 min after occlusion to obtain a steady state. Finally, a DOB infusion (3 μg/kg/min) was initiated during MI. After a stable hemodynamic state was confirmed, recordings were again obtained with Aoc. The Aoc was carefully performed to increase the LV peak systolic pressure to the identical levels in each stage.

Assessment of the pulmonary venous (PV) flow. To further examine the relation between transmitral flow and PV flow in the presence of markedly reduced LV filling at LA contraction, simultaneous recordings of PV flow volumes with transmitral flow velocity were made by an ultrasonic flowmeter (T106, Transonic Systems Inc, New York) in six additional dogs. The flowmeter was carefully placed around the upper left PV to avoid interfering with the venous flow.

Analysis of data. Micromanometric, sonomicrometric and conductance catheter signals were obtained for 15 s and digitized at 200 Hz using an on-line A to D conversion with custom software (The Codas, DATAQ Inc., Akron, Ohio) on a 32-bit microcomputer system (IBM PC/AT) during the end-expiratory portion of the respiratory cycle. The transmitral flow velocity was simultaneously recorded on paper at a speed of 100 mm/s. The average of measurements obtained from at least five consecutive beats was determined.

The following measurements and calculations were performed: peak LV pressure, LV end-diastolic pressure, LA end-diastolic pressure, peak positive and negative LV dP/dt and the time constant of LV isovolumetric pressure decay (tau). Tau was computed as the negative reciprocal of the linear regression of the natural logarithm of pressure versus

Table 1. Hemodynamic and Dimension Data

		Acute MI		
	Baseline	Aoc(−)	Aoc(+)	Aoc(+) + DOB
HR (beats/min)	104 ± 4	102 ± 6	102 ± 7	107 ± 14
LVP (mm Hg)	114 ± 15	108 ± 17	166 ± 24*‡	173 ± 26*‡
LVEDP (mm Hg)	7 ± 2	11 ± 4*	18 ± 6*‡	14 ± 4*§‖
Peak LV +dP/dt (mm Hg/s)	2,275 ± 662	1,838 ± 549	2,064 ± 542	2,674 ± 858‡¶
−dP/dt (mm Hg/s)	−2,086 ± 482	−1,702 ± 497†	−1,845 ± 399	−2,222 ± 504§¶
Tau (ms)	30 ± 7	38 ± 10†	49 ± 11*§	40 ± 11†¶
LAP (mm Hg)	9 ± 4	11 ± 3	14 ± 4*§	13 ± 5*
LAD (mm)	29 ± 4	30 ± 3*	31 ± 3*‡	30 ± 3*§
LASS (%)	6 ± 3	7 ± 3	6 ± 4	7 ± 4
CO (L/min)	1.6 ± 0.6	1.4 ± 0.3	0.9 ± 0.1*§	1.4 ± 0.3¶
K (ml^{-1})	0.10 ± 0.09	0.10 ± 0.12	0.12 ± 0.07	0.09 ± 0.05
y axis intercept (mm Hg)	−0.44 ± 1.64	−0.41 ± 2.07	−0.88 ± 1.18	0.07 ± 1.05

*$p < 0.01$; †$p < 0.05$ vs. baseline; ‡$p < 0.01$; §$p < 0.05$ vs. acute MI Aoc(−); ‖$p < 0.01$; ¶$p < 0.05$ vs. acute MI Aoc(+).
Aoc = aortic constriction; CO = cardiac output; DOB = dobutamine; HR = heart rate; K = left ventricular stiffness constant; LAD = left atrial diameter before atrial contraction; LAP = left atrial end-diastolic pressure; LASS = % left atrial systolic shortening; LV = left ventricular; LVEDP = left ventricular end-diastolic pressure; LVP = peak left ventricular pressure; LV ±dP/dt = positive and negative first derivative of left ventricular pressure; MI = myocardial ischemia; Tau = time constant of left ventricular relaxation. (Values are the mean ± SD).

time, and the LV end-diastole was determined at the time when the LV dP/dt commenced its rapid upstroke as previously reported (9). The cardiac output and the diastolic LV pressure-volume relation were determined from recordings of LV volume. The LV diastolic chamber stiffness constant was obtained by fitting the diastolic LV pressure-volume data to an exponential curve equation $P = Ae^{kV}$, where P is LV pressure, the constant A is the y axis intercept, e is the base of the natural logarithm, k is the chamber stiffness constant, and V is LV volume. The LV end-diastolic operational chamber stiffness was estimated as the ratio of developed pressure to the absolute filling volume during LA contraction. The onset of atrial contraction was picked by LA dimensional change.

The LA diameter before atrial contraction and the percent of LA systolic shortening were determined from the LA dimension. The percent of LA systolic shortening was calculated as the ratio of the change in the LA diameter during LA contraction to the LA diameter at the beginning of LA contraction.

The following measurements were obtained from the transmitral flow recordings: early diastolic peak flow velocity (E), late diastolic peak flow velocity (A), time-velocity integral of E and A and the ratio of E to A (E/A). In addition, peak (minimum) PV flow volumes during LA contraction were obtained. In experimental open-chest dogs, different from clinical findings, the PV flow during LA contraction usually moves into the LA and is not ejected from the LA backward into the PVs (10). When the backward flow volume occurred during LA contraction, it was represented by a negative value in our data process.

Statistical analysis. Data are expressed as the mean ± standard deviation. One-way analysis of variance for repeated measures was used to test for significant differences between data obtained at four states: baseline, MI without and with Aoc and DOB infusion during MI with Aoc. Fisher PLSD was used for multiple comparisons within analysis of variance. Relationship between the time-velocity integral of late diastolic transmitral flow and LV operational chamber stiffness, which was obtained from all sampled data, was assessed with linear regression analysis. A p value <0.05 was considered statistically significant.

RESULTS

Mean steady-state hemodynamic and dimension data are summarized in Table 1. Peak LV pressure was not changed at baseline, at acute MI or at DOB infusion during acute MI, whereas the Aoc resulted in a similar increase in peak LV pressure by about 55 mm Hg at each state. There were statistically no significant differences in the percent of LA systolic shortening in any condition, although the changes of LA diameter were observed.

Transmitral flow. Representative transmitral flow wave forms are shown in Figure 1. The Aoc during MI induced a significant reduction of A, indicating the development of pseudonormalization of transmitral flow velocity pattern. However, by DOB infusion during Aoc under MI, A was increased, resulting in an improvement of the LV filling during LA contraction.

Mean changes in transmitral flow velocities are provided in Table 2. Constriction of the aorta during acute MI significantly reduced A and pseudonormalized the E/A. The infusion of DOB under this condition increased A, resulting in a decreased E/A. Using the time-velocity integral of E and A, the identical changes to velocity changes were observed in all the stages.

The relations between transmitral flow and PV flow. Figure 2 shows representative simultaneous recordings of the transmitral and PV flows and recordings of LV and LA pressures during acute MI before (left) and after (mid) Aoc and with dobutamine infusion (right). In the presence of a

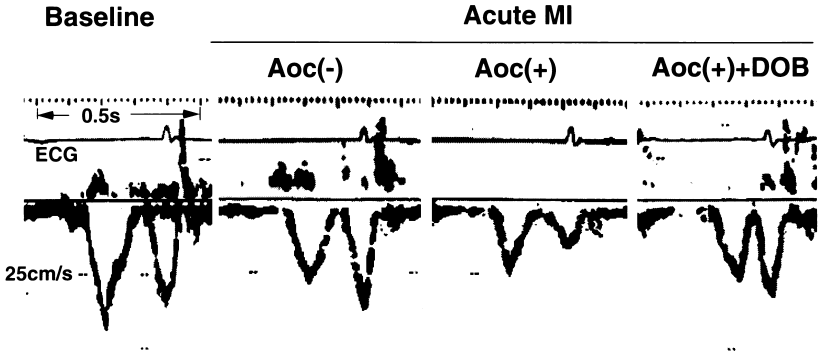

Figure 1. Transmitral flow velocity. Representative transmitral flow waveforms at baseline and during acute myocardial ischemia (MI) and acute MI with dobutamine (DOB). Aortic constriction (Aoc) during acute MI significantly reduced the late diastolic peak flow velocity, indicating pseudonormalization of the transmitral flow. Dobutamine infusion during acute MI with Aoc increased the late diastolic peak flow velocity, resulting in an improvement in left ventricular (LV) filling during left atrial (LA) contraction. ECG = electrocardiogram.

pseudonormal LV diastolic filling pattern induced by Aoc, the PV reverse flow at atrial systole was significantly increased (Fig. 2, mid). The infusion of DOB completely eliminated the PV reverse flow, accompanied by a significant increase in the late diastolic transmitral flow (Fig. 2, right). Comparative data of the peak (minimum) PV flow volume at LA contraction in each state are shown in Figure 3. With Aoc during MI, the forward PV flow at atrial systole was replaced by a significant reverse flow into the PV (from 16.7 ± 12.0 to −52.8 ± 38.1 ml/min, $p < 0.01$). However, PV flow was normalized to change from the backward flow to forward flow by DOB infusion (to 12.2 ± 19.4 ml/min, $p < 0.01$).

Changes in the diastolic LV pressure-volume relation and LV chamber stiffness. Figure 4 (top) displays representative diastolic LV pressure-volume relations at baseline, during acute MI and during acute MI with DOB infusion all before Aoc. Dobutamine infusion caused the diastolic LV pressure-volume relation to shift to the left and downward compared with that seen in MI without DOB. The LV chamber stiffness constant and the y axis intercept were not changed in any state (Table 1). Linear stiffness analysis was performed, and Figure 4 (bottom) shows changes in LV chamber stiffness at each state. The LV operational chamber stiffness was significantly increased by Aoc during MI from 1.1 ± 0.8 to 3.1 ± 2.6 mm Hg/ml ($p < 0.01$). The infusion of DOB under this condition significantly reduced the increased LV chamber stiffness to 1.7 ± 1.2 mm Hg/ml ($p < 0.05$).

Relationship between the time-velocity integral of the late diastolic transmitral flow and LV chamber stiffness. There was a significant inverse correlation between the time-velocity integral of the late diastolic transmitral flow and LV chamber stiffness (Fig. 5).

DISCUSSION

Transmitral and PV flow dynamics in the presence of LA afterload mismatch between LA and LV during atrial contraction. Figure 2 (upper mid panel) shows the simultaneous recordings of transmitral and PV flows in the presence of a pseudonormal transmitral flow pattern. We demonstrated that, although the percentage of LA systolic shortening was not changed by Aoc during acute MI, LV filling during LA contraction was significantly reduced. This resulted from an LA afterload mismatch, which was closely linked to an increase in the volume of blood ejected from the atrium backward into the PVs. The LA afterload mismatch concept in relation to LV stiffness was already reported (5). The new finding in this study, which differs from the previous report, is that the constant LA systolic performance was observed during the LA afterload mismatch accompanied by the prominent backward flow from

Table 2. Mean Changes in Transmitral Flow Velocities

		Acute MI		
	Baseline	Aoc(−)	Aoc(+)	Aoc(+) + DOB
A (cm/s)	29 ± 7	30 ± 5	22 ± 8*‡	31 ± 8‖
E (cm/s)	43 ± 7	31 ± 7*	26 ± 8*§	30 ± 9*
E/A	1.5 ± 0.2	1.0 ± 0.3†	1.4 ± 0.8§	1.0 ± 0.3†¶
Time-velocity integral of A (cm)	1.7 ± 0.4	1.8 ± 0.3	1.1 ± 0.5*‡	1.8 ± 0.5‖
Time-velocity integral of E (cm)	3.3 ± 0.5	2.2 ± 0.6*	1.6 ± 0.6*§	2.0 ± 0.8*

A = late diastolic peak velocity; Aoc = aortic constriction; DOB = dobutamine; E = early diastolic peak velocity; MI = myocardial ischemia (values are the mean ± SD).

*$p < 0.01$; †$p < 0.05$ vs. baseline; ‡$p < 0.01$; §$p < 0.05$ vs. acute MI Aoc(−); ‖$p < 0.01$; ¶$p < 0.05$ vs. acute MI Aoc(+).

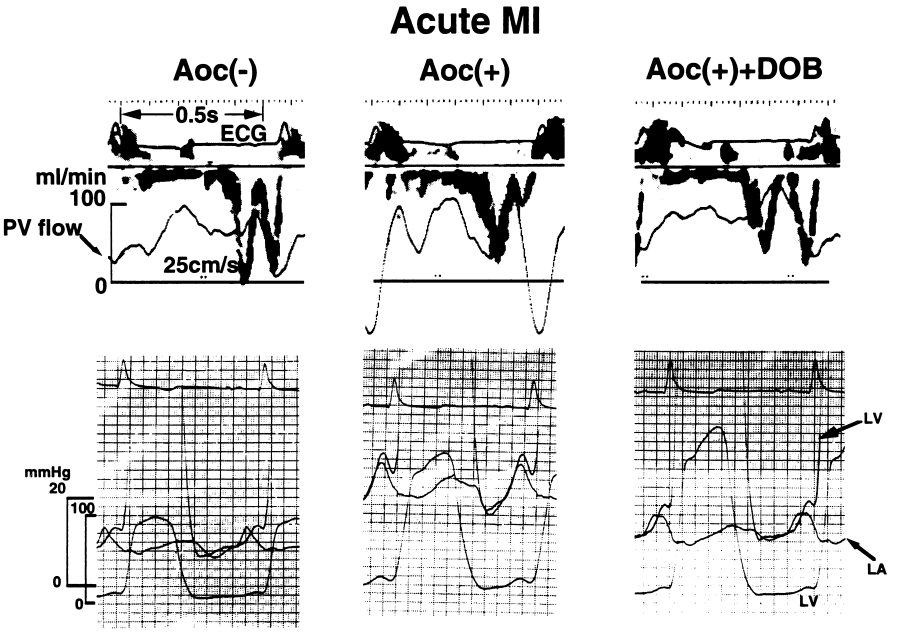

Figure 2. The relation between transmitral flow and PV venous flow and changes of LA and LV pressures with or without DOB. Representative simultaneous recordings of the transmitral flow velocity and PV flow volume and tracings of LV pressure and magnified LV and LA pressures **(arrows in right lower panel)**. With Aoc during MI, the pressure increase is larger and more rapid in the LV than it is in the LA at atrial systole **(lower mid panel)**, resulting in a reduced late diastolic transmitral flow velocity and an increased PV reverse flow volume **(upper mid panel)**. Thus, in the presence of an LA afterload mismatch, a substantial blood volume was ejected from the LA backward into the PV with atrial contraction. Dobutamine infusion markedly corrected this mismatch **(upper right panel)**. Aoc = aortic constriction; DOB = dobutamine infusion; LA = left atrial; LV = left ventricular; MI = myocardial ischemia; PV = pulmonary vein.

the LA to the PVs. This is the main feature of LA afterload mismatch in the present model.

With atrial contraction, blood is ejected from the LA into the LV determined by the positive transmitral pressure gradient (11) and also backward into the PVs. The flow in each direction is determined by the pressure gradient from the PVs to the LV, which is likely influenced by LA systolic function, LA systolic timing (12,13) and compliance of LA and LV.

Nishimura et al. (13) indicated that there was a detrimental effect of dual-chamber pacing for patients with

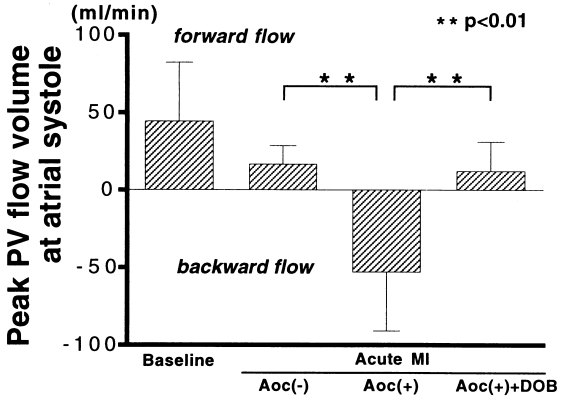

Figure 3. Changes in peak (minimum) PV flow volume during atrial contraction at each stage. The backward flow into the PV is represented by a negative value. Data are the mean ± standard deviation. Aoc = aortic constriction; DOB = dobutamine infusion; MI = myocardial infarction or ischemia; PV = pulmonary vein.

hypertrophic cardiomyopathy on LV diastolic function, particularly at the short atrioventricular interval pacing. They observed that an increase in E/A ratio and a decrease in duration of transmitral A wave in the short atrioventricular intervals (due to inadequate time for LA contraction to fill the LV) was fully associated with an increase in mean LA pressure caused by a higher residual LA volume at mitral valve closure. This is due to LA systolic timing.

Under normal circumstances, increases in pressure in the LA and the LV during atrial contraction are approximately equal, and the transmitral flow exceeds the reverse flow into the PVs. However, with reduced LV compliance and elevated filling pressures, as shown in Figure 2 (lower mid panel), the pressure increase is larger and more rapid in the LV than it is in the LA (7), resulting in a reduced transmitral flow. Thus, atrial contraction results in a marked reversal of flow into the PVs. Because of this increased reverse flow, the efficiency of LA booster pump function was significantly reduced during LA afterload mismatch for the same degree of atrial systolic shortening. On the other hand, an LV afterload mismatch can be induced by pressure loading under inadequate venous return (14), even at a stable level of myocardial contractility. The LA afterload mismatch may also occur even at a stable level of LA pump function operating before the descending limb of LA performance curve (15) because the backward flow into the PVs exceeds transmitral flow during atrial contraction. Figure 2 (upper mid panel) shows that these PV flow patterns differentiate between a high E/A ratio associated

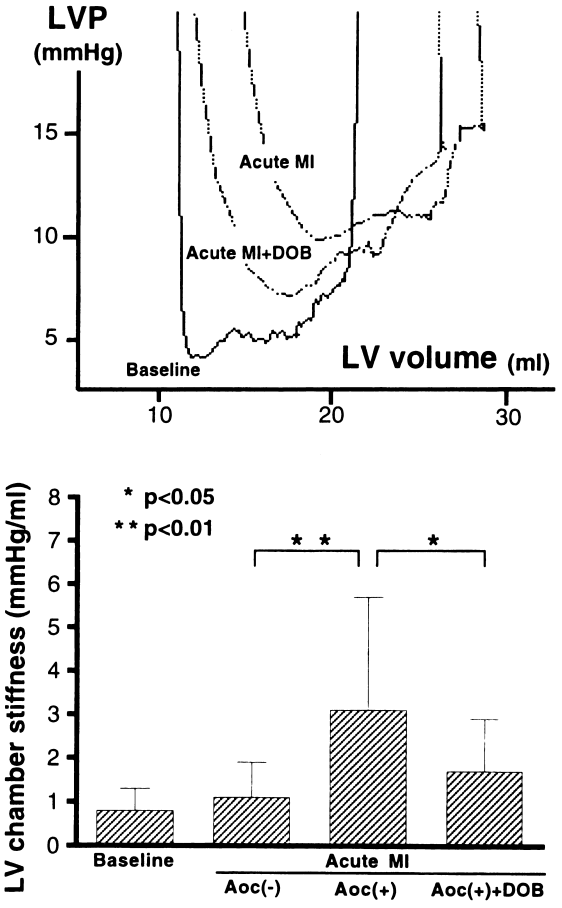

Figure 4. Changes in diastolic LVP-volume relations and changes in LV chamber stiffness at each stage. **Top:** Representative diastolic LVP-volume relations at baseline, during MI and during MI with DOB all without Aoc. **Bottom:** Changes in LV chamber stiffness at baseline, during MI and during MI with DOB, with or without Aoc. Data are the mean ± SD. Aoc = aortic constriction; DOB = dobutamine infusion; LV = left ventricle; LVP = left ventricular pressure; MI = myocardial ischemia.

with normal diastolic function characterized by a normal PV flow pattern and a high E/A ratio due to pseudonormalization associated with reduced LV compliance characterized by a PV flow pattern with a marked atrial flow reversal (2,3). Rossvoll et al. (16) reported that when the LV filling pressure was markedly increased, the pressure increase was greater and more rapid in the LV than it was in the LA, resulting in a short duration of the positive transmitral pressure gradient, and that the amount and duration of flow in each direction was determined by the transmitral and atriovenous pressure gradients. They observed a difference in the durations of PV and transmitral flow velocities during atrial contraction, which indicates an exaggerated increase in LV late diastolic pressure, caused by the increased duration of flow backward into the PVs and the decreased duration of transmitral flow. The present findings were consistent with their findings.

Mechanism of the effect of DOB on the afterload mismatch of atrial booster pump function. To explain the improvement of LA afterload mismatch by DOB, at least two

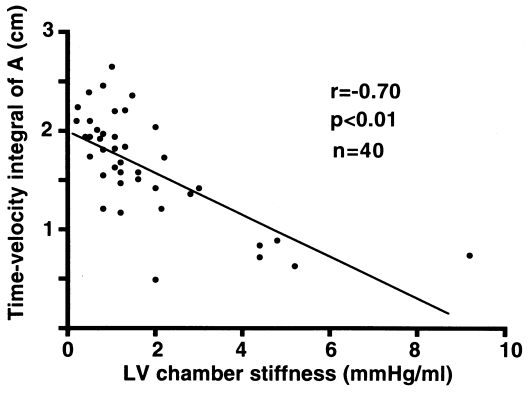

Figure 5. Relationship between the time-velocity integral of the A and LV operational chamber stiffness for all the data points in this study. A = late diastolic transmitral flow velocity; LV = left ventricle.

possible mechanisms should be considered. Left atrial systolic function may be increased by DOB or, if DOB improves LV compliance, LA afterload during LA contraction would be reduced. In this study, the percent of LA systolic shortening was not significantly changed throughout the study even by DOB infusion. Thus, a significant alteration in LA booster pump function seems unlikely to be induced by an augmentation of LA contractility during DOB infusion.

Afterload on the LA is primarily determined by LV chamber stiffness and LV pressure just before the onset of LA contraction. When diastolic pressure is elevated, the operational chamber stiffness of the LV is increased because it functions on a steeper portion of its pressure-volume curve. We demonstrated that DOB infusion caused the diastolic LV pressure-volume relation during acute MI to shift to the left and downward. We monitored LV chamber stiffness, calculated as the ratio of developed pressure to the absolute filling volume during LA contraction, throughout the experiment. Dobutamine significantly reduced the markedly increased LV chamber stiffness during LA afterload mismatch, whereas no significant changes in the LV chamber stiffness constant and the y axis intercept were observed in any state of this study. The change in the pressure-volume relation may not be due to a change in myocardial compliance, but rather to a shift in the position of the pressure-volume curve on the diastolic LV pressure-volume relationship. These findings suggest that DOB reduced the afterload on LA. Carroll et al. (17) reported that DOB reduced the LV diastolic pressure without significant changes in the LV chamber stiffness constant and caused a left-downward shift in the same diastolic pressure-diameter relation (due to the reduced end-systolic chamber size) and reduced the minimum diastolic pressure in patients with congestive cardiomyopathy. Other investigators have reported similar findings (18–21). Based on these data, we propose that the DOB-induced correction of LA afterload mismatch did not result from an alteration of LA systolic function but rather from an improvement in the efficiency of the LA booster pump function by a reduction of the afterload on LA.

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Relationship between the time-velocity integral of late diastolic transmitral flow and LV operational chamber stiffness. In situations in which LV compliance is markedly decreased, such as constrictive pericarditis and restrictive cardiomyopathy, most abnormal LV filling pattern, so called "restricted" LV filling pattern, has been observed and is characterized by a tall, narrow early filling wave in association with a high-peak velocity and a shortened deceleration time caused by an abnormally rapid increase in early diastolic LV pressure and a small atrial filling wave (3,22). Myocardial ischemia is associated with an immediate decrease in myocardial compliance (23–25). So, it is expected that the filling pattern observed in this study in dogs with afterloading induced by Aoc during MI, which was attributed to much lower LV chamber compliance than that solely due to MI, will resemble the filling behavior seen in the markedly elevated LV filling pressure associated with the "restricted" LV filling pattern. This finding is in agreement with a previous report from our group (7). We previously demonstrated that, in patients with old MI, the increase in LV operational chamber stiffness induced by acute pressure load during angiotensin infusion significantly reduced LV filling during atrial contraction, resulting from an afterload mismatch of LA booster pump function, and that there was an inverse correlation between LV filling volume at atrial contraction and LV chamber stiffness. In this study a significant inverse correlation between the time-velocity integral of the late diastolic transmitral flow and the LV operational chamber stiffness was observed under the same percentage of LA systolic shortening. This relationship suggests that the LV operational chamber stiffness plays an important role in affecting the efficiency of LA booster pump function.

Study limitations. In this study measurements of LA volume were only based on the anteroposterior dimension. This is a limitation of the study because dimensional changes during atrial contraction may be dissimilar in different dimensions (26). However, this limitation might be counterbalanced by identical methodology during measurements on the basis of percentage of shortening ratio in different phases of the protocol.

Conclusions. Dobutamine improved the afterload mismatch of LA booster pump function associated with pseudonormalization of the transmitral flow velocity pattern during acute MI with afterloading. This effect may have been due to a reduction in LV operational chamber stiffness at late diastole (reduction of LA afterload) induced by DOB, leading to an increase in the LA forward ejection into the LV associated with a decrease in backward flow volume into the PVs during atrial contraction.

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